DECLARATION OF DR. BRUCE WHITELAW

I, Christopher Bruce Alexander Whitelaw, declare as follows:

1. I am an inventor of the invention claimed in US Patent Application No. 10/522,536, derived from International Patent Application No. PCT/GB2003/003192, filed on 25 July 2003.

2. I obtained an honours degree in Biology in 1982 from the University of Edinburgh, UK and a PhD on the analysis of the transcriptional control domains of the human c-*myc* proto-oncogene in 1986 from the University of Glasgow, UK. I have been the Head of the Division of Developmental Biology at the Roslin Institute, Edinburgh, UK since 2005. I am currently the Editor-in-Chief of the publication Transgenic Research and the co-director of the Scottish Network of Excellence for the Development of Novel Technologies to Fight Viral Disease in Farm Animals. I have authored or co-authored a large number of papers regarding cloning techniques and transgenic animals. My curriculum vitae including a list of these publications is enclosed herewith as Appendix A.

3. Currently, I am Head of the Division of Developmental Biology at the Roslin Institute, Edinburgh, UK.

4. I am familiar with the above-referenced patent application and the Office Action dated 14 December 2007. I understand that objections have been raised under 35 USC §112 and that the Examiner considers that the claims do not comply with the written description requirement or the enablement requirement. I understand that the claims that have been examined are directed to a method of detecting a gene activation event *in vivo* by assaying a transgenic non-human animal whose cells express a construct comprising a nucleic acid sequence encoding a beta-lactoglobulin (BLG) under the control of the Cyp1a1 promoter and a nucleic acid sequence encoding a peptide sequence having the sequence of SEQ ID NO. 1, wherein the animal is subjected to a gene activation event of toxicologically induced stress, and a method of screening for, or monitoring of toxicologically induced stress by using said transgenic non-human animal. I understand that the claims have now been limited to transgenic rodents.

5. The Examples of the present application provide sufficient information to a person of skill in the art to produce a transgenic rodent as now claimed for use in the present invention.

6. In particular, Example 11 gives guidance regarding the expression of epitope tagged lipocalin reporter proteins in transgenic animals. Example 11 teaches that transgenic animals can be generated using one of several standard methods in the art including pronuclear injection, blastocyst injection of transfected cells or using viral vectors. These methods were well known in the art at the priority date of the present invention and a skilled person would readily be able to carry out these methods using their knowledge and the teachings of the scientific papers referred to on page 48, lines 15 to 19 of the present application.

7. Example 11 also gives specific guidance as to how to product transgenes containing the Cyp1a1 promoter sequence driving expression of myc epitope tagged BLG reporter, as described on page 48, line 25 to page 49, line 7.

8. The present application also gives guidance as to how to identify positive transgenic animals by analysis of DNA. Page 49, lines 9 to 15 of the present application also demonstrates how to detect and screen for a gene activation event of toxicologically induced stress. In particular, page 49, lines 10 to 15 specify that transgenic animals are exposed to stress, for example by drug administration, and blood and urine samples are collected over time. Samples collected pre- and post-insult are analysed for the presence of the tagged lipocalin by methods including Western blot and ELISA. Depending on the specific insult or inducing agent an increase or decrease in reporter activity are detected.

9. The Cyp1a1 promoter is also well described and characterised in the art, for example in WO 97/23635.

10. It is thus my opinion that one skilled in this field would be able to put the invention into practice using the disclosure of the present application and would believe that the inventors had possession of the invention now claimed.

Date 8th May 2008

Christopher Bruce Alexander Whitelaw.